General

Guideline Title

Kidney disease in HIV-infected patients.

Bibliographic Source(s)

New York State Department of Health. Kidney disease in HIV-infected patients. New York (NY): New York State Department of Health; 2012 Sep. 21 p. [54 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

The quality of evidence (I-III) and strength of recommendation (A-C) are defined at the end of the "Major Recommendations" field.

Introduction

Key Point:

Human immunodeficiency virus (HIV)-infected black patients with chronic kidney disease (CKD) have a significantly higher risk for end-stage renal disease (ESRD) compared with HIV-infected white patients with CKD.

Patient Education about Kidney Disease

Clinicians should educate patients about the following (BIII):

- The association between HIV and kidney disease
- The role of antiretroviral therapy (ART) in prevention of HIV-associated nephropathy (HIVAN)
- Importance of routine monitoring appointments to assess for other causes of kidney disease

Renal Syndrome and Risk Factors for Kidney Disease

See Appendix A and Appendix B in the original guideline document for information about the reported prevalence of acute renal failure (ARF) and the reported prevalence of CKD, respectively.

Routine Kidney Disease Screening: Laboratory Assessment

Clinicians should routinely assess kidney function in all HIV-infected patients. A renal assessment should include:

- Glomerular filtration rate (GFR) estimated from serum creatinine (baseline and at least every 6 months) (AII)
- Blood urea nitrogen (baseline and at least every 6 months) (AIII)
- Urinalysis (baseline and at least annually) (AIII)
- For patients with diabetes and no known proteinuria: calculation of urine albumin-to-creatinine ratio to detect microalbuminuria (baseline and at least annually) (AI)

For patients receiving a tenofovir-containing regimen, clinicians should estimate glomerular filtration rate at initiation of therapy, 1 month after initiation of therapy, and at least every 4 months thereafter.

Glomerular Filtration Rate

Important Limitations to Calculating GFR

- Unlike the Chronic Kidney Disease Epidemiology Consortium (CKD-EPI), the Modification of Diet in Renal Disease (MDRD) and Cockcroft-Gault have not been validated in people with normal kidney function and do not accurately estimate GFR in the normal range; therefore, when GFR is >60 mL/min, small but possibly meaningful changes in GFR that may indicate early kidney disease cannot be reliably measured with the MDRD and Cockcroft-Gault equations.
- All of these equations have diminished accuracy in patients with extremes of body weight, such as body builders, amputees, and frail individuals; for these patients, a 24-hour creatinine clearance may be a better test because serum creatinine within the normal range may not correlate with a normal GFR.

Key Points:

- The MDRD or CKD-EPI, not the Cockcroft-Gault, equations are used by clinical laboratories when reporting estimated GFR from serum creatinine; however, drug manufacturers' recommended dose adjustments for kidney function are based on the Cockcroft-Gault equation, not the MDRD.
  - For MDRD and CKD-EPI calculators, refer to http://mdrd.com
  - For Cockcroft-Gault, refer to http://nephron.com/cgi-bin/CGSI.cgi
- The CKD-EPI equation has begun to replace the MDRD equation when clinical laboratories report GFR. Unlike the other equations, the CKD-EPI equation has been validated in individuals with normal kidney function of >60 mL/min, although this has not been studied in the setting of HIV infection.

Urine Protein Excretion

Key Point:

Microscopic hematuria and mild proteinuria (urinary protein excretion <1500 mg/day) are generally asymptomatic. They have little clinical impact alone but can indicate an early stage of a serious disease, such as acute or chronic glomerular disease. A kidney biopsy is often deferred in such circumstances until the renal disease progresses, as manifested by increasing proteinuria, decreasing GFR, or the development of hypertension.

Diagnosis and Evaluation of Kidney Disease

All patients with borderline glomerular filtration rate, regardless of age, should undergo the following diagnostic evaluation of kidney function (AII):

- Urinalysis to screen for cells and cellular casts
- Quantification of urinary protein excretion
- Renal sonogram

- Careful physical examination

Primary care clinicians should refer patients to a nephrologist when (AII):

- The diagnosis is uncertain
- Kidney disease is progressing rapidly
- Stage 4 to 5 chronic kidney disease is present (see Table 1 in the original guideline document)
- Kidney biopsy is being considered

Key Point:

As CKD progresses, more pronounced signs or symptoms may appear, including increased blood pressure, anemia, or edema (mild to severe). All forms of CKD have the potential to progress to ESRD.

Diagnosis of HIV Associated Nephropathy

In circumstances when a kidney biopsy is not performed for an HIV-infected patient with kidney dysfunction, because of contraindication, clinician judgment, or patient preference, the following diagnostic criteria for HIV-associated nephropathy are reasonable (BIII):

- No other explainable cause(s) of kidney disease *and*
- Proteinuria of >2000 mg *and*
- Normal to large echogenic kidneys on sonogram *and*
- Black race

For patients with empirically diagnosed HIV-associated nephropathy whose kidney disease worsens after initiation of ART, a biopsy should be performed to determine the underlying cause. (AIII)

Management of Kidney Disease

Patients with low-grade proteinuria and/or slightly decreased glomerular filtration rate should receive ART if not already receiving it, an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, and careful monitoring of kidney function.

Clinicians should consult with a nephrologist when managing patients who are approaching end-stage renal disease due to stage 4 to 5 chronic kidney disease (see Table 1 in the original guideline document) and require special interventions for hyperparathyroidism, anemia, hemodialysis vascular access, peritoneal dialysis, and/or kidney transplant options. (AII)

Use of ART to Prevent Progression of Kidney Disease

Clinicians should educate patients with HIV-associated nephropathy about the increased urgency of initiating ART (see the National Guideline Clearinghouse [NGC] summary of the New York State Department of Health [NYSDOH] guideline Antiretroviral Therapy: Section III: Deciding When to Initiate ART). (AII)

Management of Comorbid Hyperglycemia, Dyslipidemia, Anemia, and Hypertension

Clinicians should treat hyperglycemia, dyslipidemia, anemia, and hypertension in HIV-infected patients with kidney disease according to standard guidelines for non-HIV-infected patients. (AI)

HIV-infected normotensive patients with kidney disease should receive angiotensin-converting enzyme inhibitors or angiotensin receptor blockers according to standard guidelines for non-HIV-infected patients. (AI)

Management Considerations Requiring Referral to a Nephrologist

Clinicians should refer HIV-infected patients with kidney disease to a nephrologist when:

- Considering management with steroids, immunosuppression, hemodialysis, or transplantation (AIII)
- A diagnosis of membranoproliferative glomerulonephritis has been made for HIV/hepatitis C virus (HCV) co-infected patients (AIII)

HIV-Related Medication Adjustments in the Setting of Renal Complication

Clinicians should determine whether dose adjustments are required for certain antiretroviral agents or whether patients should avoid use of certain agents when glomerular filtration rate reaches ≤50 mL/min; recommendations for such considerations are provided in the table below. (AIII)

Table: Recommended ART Dose Adjustments at GFR ≤50 mL/min[a]	
Nucleoside/Nucleotide Reverse Transcriptase Inhibitors	
• Zidovudine	• Adjust dose if creatinine clearance reaches ≤15 mL/min
• Didanosine[b] • Emtricitabine • Lamivudine • Stavudine • Tenofovir[c]	• Adjust dose if creatinine clearance reaches ≤50 mL/min • Avoid or use with caution when didanosine is co-administered with tenofovir in renal failure
CCR5 Co-Receptor Agonists	
• Maraviroc	• Adjust dose if creatinine clearance reaches <30 mL/min and patient experiences postural hypotension
Co-Formulated Agents	
• Combivir (lamivudine + zidovudine) • Epzicom (abacavir + lamivudine) • Trizivir (abacavir + lamivudine + zidovudine) • Atripla (efavirenz + emtricitabine + tenofovir[c]) • Complera (emtricitabine + rilpivirine + tenofovir[c]) • Stribild[d] (elvitegravir + cobicistat + emtricitabine + tenofovir[c])	• Do not use if creatinine clearance reaches <50 mL/min • Individual components should be administered with appropriate dose adjustments
• Truvada (emtricitabine + tenofovir[c])	Do not use if creatinine clearance reaches <30 mL/min

[a] Clinicians should refer to prescribing information for individual agents when a patient has reduced GFR.

[b] The manufacturer recommends adjustment at ≤60 mL/min for didanosine; however, adjustment at ≤50 mL/min is a reasonable approach.

[c] Alternative antiretroviral agents should be considered in patients with renal insufficiency.

[d] Avoid use in patients with creatinine clearance of <70 mL/min at initiation of treatment.

Tenofovir

For patients receiving tenofovir-containing regimens, clinicians should:

- Estimate glomerular filtration rate at initiation of therapy, 1 month after initiation of therapy, and at least every 4 months thereafter (BII)
- Adjust tenofovir dosing when glomerular filtration rate approaches 50 mL/min or discontinue tenofovir according to clinical status (AII)
- Withhold tenofovir until all potential causes have been determined in patients who develop acute renal failure (BII)

Nonsteroidal Anti-inflammatory Drugs

Clinicians should assess for use of nonsteroidal anti-inflammatory drugs in HIV-infected patients with declining renal function. Decisions about the use of such agents for these patients should be individualized and patients should be educated about the importance of using these drugs with caution. (BII)

Definitions:

Quality of Evidence for Recommendation

I. One or more randomized trials with clinical outcomes and/or validated laboratory endpoints
II. One or more well-designed, non-randomized trials or observational cohort studies with long-term clinical outcomes
III. Expert opinion

Strength of Recommendation

A. Strong recommendation for the statement
B. Moderate recommendation for the statement
C. Optional recommendation

Clinical Algorithm(s)

An algorithm is provided in the original guideline document for "Steps for screening and initial management of kidney disease."

Scope

Disease/Condition(s)

Human immunodeficiency virus (HIV) infection
Human immunodeficiency virus-associated nephropathy (HIVAN)
Chronic kidney disease
Acute renal failure
Membranoproliferative glomerulonephritis (MPGN)

Guideline Category

Counseling

Diagnosis

Evaluation

Management

Prevention

Risk Assessment

Screening

Treatment

Clinical Specialty

Allergy and Immunology

Family Practice

Infectious Diseases

Internal Medicine

Nephrology

Intended Users

Advanced Practice Nurses

Clinical Laboratory Personnel

Health Care Providers

Nurses

Physician Assistants

Physicians

Public Health Departments

Guideline Objective(s)

To develop guidelines for diagnosis and management of kidney disease in human immunodeficiency virus (HIV)-infected patients

Target Population

Human immunodeficiency virus (HIV)-infected patients at risk of or diagnosed with kidney disease

Interventions and Practices Considered

Screening/Diagnosis/Evaluation/Initial Management

1. Patient education about human immunodeficiency virus (HIV) and kidney disease
2. Routine screening assessment of kidney function
    - Glomerular filtration rate (GFR) estimated from serum creatinine
    - Blood urea nitrogen
    - Urinalysis
    - Calculation of urine albumin-to-creatinine ratio in patients with diabetes
3. Diagnostic evaluation of kidney function
    - Urinalysis to screen for cells and cellular casts
    - Quantification of urinary protein excretion
    - Renal sonogram
    - Careful physical examination
4. Referral to nephrologist when disease progression indicates
5. Kidney biopsy

Management/Treatment

1. Antiretroviral therapy (ART) to prevent progression of kidney disease
2. Angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB)
3. Careful monitoring of kidney function
4. Nephrologist consultation, as needed

5. Management of comorbid hyperglycemia, dyslipidemia, anemia, and hypertension
6. HIV-related medication dosage adjustments in the setting of renal complications
7. Special considerations for patients receiving tenofovir-containing regimens
8. Assessing patients for use of nonsteroidal anti-inflammatory drugs

Major Outcomes Considered

- Prevalence of acute renal failure and chronic renal disease among human immunodeficiency virus (HIV)-infected patients
- Effect of antiretroviral therapy on survival rate and kidney function in patients with HIV-associated nephropathy

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

MEDLINE was searched through May 2012 using key words appropriate to the topic. Available guidelines from the National Kidney Foundation on kidney disease that did not specifically pertain to HIV infection were also reviewed. Additionally, National Institutes of Health annual data reports on chronic kidney disease and end-stage renal disease, and administrative and cohort data published on the subject were used to consider disease estimates.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus (Committee)

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence for Recommendation

I. One or more randomized trials with clinical outcomes and/or validated laboratory endpoints
II. One or more well-designed, non-randomized trials or observational cohort studies with long-term clinical outcomes
III. Expert opinion

Methods Used to Analyze the Evidence

Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

AIDS Institute clinical guidelines are developed by distinguished committees of clinicians and others with extensive experience providing care to people with HIV infection. Committees* meet regularly to assess current recommendations and to write and update guidelines in accordance with newly emerging clinical and research developments.

The Committees* rely on evidence to the extent possible in formulating recommendations. When data from randomized clinical trials are not available, Committees rely on developing guidelines based on consensus, balancing the use of new information with sound clinical judgment that results in recommendations that are in the best interest of patients.

* Current committees include:

- Medical Care Criteria Committee
- Committee for the Care of Children and Adolescents with HIV Infection
- Dental Standards of Care Committee
- Mental Health Guidelines Committee
- Committee for the Care of Women with HIV Infection
- Committee for the Care of Substance Users with HIV Infection
- Physicians' Prevention Advisory Committee
- Pharmacy Advisory Committee

Rating Scheme for the Strength of the Recommendations

Strength of Recommendation

A. Strong recommendation for the statement
B. Moderate recommendation for the statement
C. Optional recommendation

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

All guidelines developed by the Committee are externally peer reviewed by at least two experts in that particular area of patient care, which ensures depth and quality of the guidelines.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for selected recommendations (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate diagnosis, management and prevention of kidney disease in human immunodeficiency virus (HIV)-infected patients

Potential Harms

- Tenofovir is associated with renal dysfunction. It should be dose-adjusted according to glomerular filtration rate (GFR) or discontinued according to clinical status.
- Use of nonsteroidal anti-inflammatory drugs (NSAIDs) may exacerbate kidney disease. NSAID use should be assessed, and these agents should be used with caution in the setting of declining renal function.
- Clinicians should be aware of the potential for significant drug-drug interactions between antiretroviral therapy (ART) and immunosuppressive agents.

Contraindications

Contraindications

- Tenofovir is relatively contraindicated as an initial regimen in patients with preexisting kidney disease and glomerular filtration rate (GFR) levels near 50 to 60 mL/min.
- Concomitant use of nephrotoxic agents should be avoided in patients with renal dysfunction.

Qualifying Statements

Qualifying Statements

When formulating guidelines for a disease as complex and fluid as human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS), it is impossible to anticipate every scenario. It is expected that in specific situations, there will be valid exceptions to the approaches offered in these guidelines and sound reason to deviate from the recommendations provided within.

Implementation of the Guideline

Description of Implementation Strategy

The AIDS Institute's Office of the Medical Director directly oversees the development, publication, dissemination and implementation of clinical practice guidelines, in collaboration with The Johns Hopkins University, Division of Infectious Diseases. These guidelines address the medical management of adults, adolescents and children with human immunodeficiency virus (HIV) infection; primary and secondary prevention in medical settings; and include informational brochures for care providers and the public.

Guidelines Dissemination

Guidelines are disseminated to clinicians, support service providers and consumers through mass mailings and numerous AIDS Institute-sponsored

educational programs. Distribution methods include the HIV Clinical Resource website, the Clinical Education Initiative (CEI), the AIDS Educational Training Centers (AETC) and the HIV/AIDS Materials Initiative. Printed copies of clinical guidelines are available for order from the New York State Department of Health (NYSDOH) Distribution Center for providers who lack internet access.

Guidelines Implementation

The HIV Clinical Guidelines Program works with other programs in the AIDS Institute to promote adoption of guidelines. Clinicians, for example, are targeted through the CEI and the AETC. The CEI provides tailored educational programming on site for health care providers on important topics in HIV care, including those addressed by the HIV Clinical Guidelines Program. The AETC provides conferences, grand rounds and other programs that cover topics contained in AIDS Institute guidelines.

Support service providers are targeted through the HIV Education and Training initiative which provides training on important HIV topics to non-physician health and human services providers. Education is carried out across the State as well as through video conferencing and audio conferencing.

The HIV Clinical Guidelines Program also works in a coordinated manner with the HIV Quality of Care Program to promote implementation of HIV guidelines in New York State. By developing quality indicators based on the guidelines, the AIDS Institute has created a mechanism for measurement of performance that allows providers and consumers to know to what extent specific guidelines have been implemented.

Finally, best practices booklets are developed through the HIV Clinical Guidelines Program. These contain practical solutions to common problems related to access, delivery or coordination of care, in an effort to ensure that HIV guidelines are implemented and that patients receive the highest level of HIV care possible.

Implementation Tools

Clinical Algorithm

Resources

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

New York State Department of Health. Kidney disease in HIV-infected patients. New York (NY): New York State Department of Health; 2012 Sep. 21 p. [54 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012 Sep

Guideline Developer(s)

New York State Department of Health - State/Local Government Agency [U.S.]

Source(s) of Funding

New York State Department of Health

Guideline Committee

Medical Care Criteria Committee

Composition of Group That Authored the Guideline

Committee Chair: Judith A Aberg, MD, New York University School of Medicine, New York, New York

Committee Vice-Chair: Samuel T Merrick, MD, New York-Presbyterian Hospital, Weill Cornell Medical Center, New York, New York

Members: Bruce D Agins, MD, MPH, New York State Department of Health, AIDS Institute, New York, New York; Barbara Chaffee, MD, MPH, United Health Services, Binghamton, New York; Steven M Fine, MD, PhD, University of Rochester Medical Center, Rochester, New York; Barbara E Johnston, MD, Mount Sinai Comprehensive Health Program-Downtown, New York, New York; Jessica E Justman, MD, Mailman School of Public Health, Columbia University, New York, New York; Jason M Leider, MD, PhD, North Bronx Healthcare Network of Jacobi and North Central Bronx Hospitals, Bronx, New York; Joseph P McGowan, MD, FACP, North Shore University Hospital, Manhasset, New York; Rona M Vail, MD, Callen-Lorde Community Health Center, New York, New York; Barry S Zingman, MD, Montefiore Medical Center and Albert Einstein College of Medicine, Bronx, New York

AIDS Institute Staff Liaison: Demetre C Daskalakis, MD, Bellevue Hospital, NYU Langone Medical Center, New York, New York

AIDS Institute Staff Physicians: Charles J Gonzalez, MD, New York State Department of Health, AIDS Institute, New York, New York; Cheryl A Smith, MD, New York State Department of Health, AIDS Institute, New York, New York

Department of Veterans Affairs Medical Center Liaison: Sheldon T Brown, MD, James J Peters Veteran Affairs Medical Center, Bronx, New York

Medical Society of the State of New York Liaison: William Valenti, MD, FIDSA, University of Rochester School of Medicine, Rochester, New York

New York City Department of Health and Mental Hygiene Liaison: Blayne Cutler, MD, PhD, New York City Department of Health and Mental Hygiene, Long Island City, New York

New York City Health and Hospitals Corporation Liaison: Joseph R Masci, MD, Elmhurst Hospital Center, Elmhurst, New York

New York State Department of Correctional Services Liaisons: Douglas G Fish, MD, Albany Medical College, Albany, New York; Carl J Koenigsmann, MD, New York State Department of Correctional Services, Albany, New York

Pharmacy Advisory Committee Liaison: John M Conry, PharmD, BCPS, AAHIVP, Saint John's University, Queens, New York

HIV Quality of Care Advisory Committee Liaison: Peter G Gordon, MD, Columbia University College of Physicians, and Surgeons, New York, New York

Principal Investigator: John G Bartlett, MD, Johns Hopkins University, School of Medicine, Baltimore, Maryland

Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the New York State Department of Health AIDS Institute Web site .

Availability of Companion Documents

The following are available:

- Preventing and managing kidney disease in HIV-infected patients. CME course. Available from the Clinical Education Initiative Web site .
- Kidney and liver transplantation in people with HIV. Video. Available from the Clinical Education Initiative Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on February 21, 2013. This summary was updated by ECRI Institute on September 18, 2015 following the U.S. Food and Drug Administration advisory on non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs).

Copyright Statement

Disclaimer

NGC Disclaimer

The National Guideline Clearinghouseâ„¢ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion-criteria.aspx.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.